European Food Safety Authority

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SCIENTIFIC OPINION

Updating the opinion related to the revision of Annexes II and III to Council Directive 91/414/EEC concerning the placing of plant protection products on the market – Toxicological and metabolism studies[1]

Prepared by the Panel on Plant Protection Products and their Residues (PPR)

(Question No EFSA-Q-2009-00615)

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PANEL MEMBERS

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SUMMARY

The European Food Safety Authority (EFSA) asked its Panel on Plant Protection Products and their Residues to review the Opinions of the PPR Panel issued in 2006 and 2007 related to the revision of Annexes II and III to Council Directive 91/414/EEC (data requirements) concerning the placing of plant protection products on the market.

The present opinion is an update to the existing opinion on Annex II & III – Toxicological and metabolism studies (EFSA, 2007).

The PPR Panel considers that there are no relevant new scientific findings, test guidelines or guidance documents in the field of toxicology that presently merit an update of the previous opinion. Consequently an in-depth review is neither needed nor is it feasible, considering the short timeline given for the mandate. In this context the PPR Panel draws attention to the recent opinion on existing approaches incorporating replacement, reduction and refinement of animal testing: applicability in food and feed risk assessment (EFSA, 2009). In addition, revision of the data requirements may be necessary when three currently on-going activities of the PPR Panel are finalised (i.e. development of a guidance document for pesticide exposure assessment for workers, operators, bystanders and residents, a guidance document for the

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residue definition of pesticide metabolites, and a revision of the guidance document on dermal absorption).

It will also be necessary to define additional data requirements to address certain issues e.g. certain pesticides which may disrupt the endocrine system, safeners, co-formulants and synergists, once the new Regulation on the placing of plant protection products on the market is in place.

In addition to that, the PPR Panel cannot at present give a definitive statement on whether or not the data requirements given in Annex II and III are sufficient to gauge risks of nanopesticides, since such an assessment would require substantial scientific effort and time, which could not be provided within the frame of the present mandate.

The PPR Panel emphasises that the recommendations given in the previous opinion still stand.

Key words: Annex II and III, data requirements, Directive 91/414/EEC, plant protection products, pesticides, toxicology

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BACKGROUND AS PROVIDED BY EFSA

In November 2005, the Commission informed EFSA[2] that they were revising the data requirements for the authorisation of active substances and plant protection products in the framework of Council Directive 91/414/EEC. The revision process involved Part A of Annexes II and III and had been organised in order to amend the directives[3] laying down the data requirements for active substances and plant protection products. The Commission had prepared SANCO Working Documents[4] containing the proposed data requirements to revise Annexes II and III to Directive 91/414/EEC and asked the PPR Panel to provide observations and/or possible recommendations, and in particular to verify that the methodology and the approaches presented in the draft data requirements were in line with the scientific state of the art in the relevant field and the extent of its applicability with respect to the risk assessment of plant protection products.

Between May 2006 and March 2007, upon request of the Commission, the PPR Panel issued six opinions on the SANCO working documents related to the revision of Annexes II and III to Council Directive 91/414/EEC concerning the placing of plant protection products on the market (EFSA 2006a, b, c; EFSA 2007a, b, c).

Until now the Annexes II and III to Council Directive 91/414/EEC have not been finally amended, but meanwhile a new regulation of the European Parliament and of the Council on the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC has been elaborated and will enter into force in 2009.

Following Art 8(4) of this new regulation, the data requirements shall contain the requirements for active substances and plant protection products as set out in Annexes II and III to Directive 91/414/EC and laid down in further regulations to be adopted.

Therefore, the PPR Panel would like to revisit their opinions issued in 2006 and 2007 to make sure that the data requirements for active substances and plant protection products are up to date at the time of their adoption under the relevant regulation.

[2] Letters P. Testori Coggi 21 Nov 2005 (requesting opinions on phys-chem. properties, analytical methods, residues); 03 Aug 2006 (fate and behaviour, toxicological and metabolism studies); 29 Sept 2006 (ecotoxicological studies)

[3] 94/37/EC physical and chemical properties; 96/46/EC analytical methods; 94/79/EC toxicological and metabolism studies; 96/68/EC residues; 95/36/EC fate and behaviour in the environment; 96/12/EC ecotoxicological studies.

[4] SANCO 10438, 10439, 10440, 10481, 10482, 10483

TERMS OF REFERENCE AS PROVIDED BY EFSA

The Scientific Panel on Plant Protection Products and their Residues is asked by EFSA to review the Opinions of the PPR Panel issued in 2006 and 2007 related to the revision of Annexes II and III to Council Directive 91/414/EEC concerning the placing of plant protection products on the market.

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EVALUATION

1. Introduction

In 2006 - 2007, the PPR Panel reviewed the proposed revisions of toxicological data requirements in Annex II and III of Directive 91/414/EEC, as set out in Commission Working Document, SANCO/10482/2006 and issued an opinion on the subject on 31 January 2007 (EFSA, 2007). At that time, in addition to specific comments and recommendations on various sections of the draft data requirements, the PPR Panel formulated a set of main recommendations.

2. Opinion

The PPR Panel considers that there are no relevant new scientific findings, test guidelines or guidance documents in the field of toxicology that presently merit an update of the previous opinion. Therefore an in-depth review is neither needed nor feasible considering the short timeline given for the mandate.

However, the Panel is currently working on several activities concerning the development or updating of guidance documents, e.g. GD for pesticide exposure assessment for workers, operators, bystanders and residents, GD on dermal absorption, toxicological relevance of metabolites and degradates of pesticides active substances for dietary risk assessment. When these GDs are finalized and adopted by MS/Commission, a revision of the data requirements may be necessary. Moreover, when the new Regulation of the European Parliament and of the Council on the placing of plant protection products on the market is in place, it will be necessary to come back to the Annexes to define additional requirements to address certain issues e.g. pesticides which may disrupt the endocrine system, safeners, co-formulants and synergists.

The panel wishes to emphasise that endocrine disruption is one expression of toxic effects, among others, where changes in for instance growth and development may be observed at various concentration thresholds (i.e. from maternotoxic concentrations for the least potent disruptors to very low concentrations for the most potent disruptors).

The PPR Panel emphasises that the recommendations given in the previous opinion still stand.

The PPR Panel also wishes to draw attention to the opinion of the Scientific Committee on "Existing approaches incorporating replacement, reduction and refinement of animal testing: applicability in food and feed risk assessment" (EFSA, 2009a). In this opinion, for each toxicological endpoint, a description is given of the current test methods in use, which is followed by an overview of the recent and likely future developments in terms of the Three Rs for regulatory purposes.

Although so far there are no registered pesticides on the market which contain nanomaterials, progress of science indicates that this might not be the case in the future, in particular since there are already biocides with these characteristics. Regarding the assessment of risks in nanotechnology, the Commission's independent Scientific Committee on Emerging and

Newly Identified Health Risks (SCENIHR) has already published several opinions (SCENIHR 2006, 2007, 2009). The latest one, published in January 2009, indicates that methodologies to assess exposure to manufactured nanomaterials to humans and the environment and the identification of potential hazards require further development, that more research is needed, and that risk assessment should be performed case by-case for each nanomaterial.

Also EFSA's Scientific Committee (SC) has already published a scientific opinion on nanoscience and nanotechnologies in relation to food and feed safety (EFSA, 2009b). The SC concluded that established international approaches to risk assessment can also be applied to engineered nanomaterials. A case-by-case approach would be necessary as in practice, current data limitations and a lack of validated test methodologies could make risk assessment of specific nanoproducts very difficult and subject to a high degree of uncertainty.

The PPR Panel is of the opinion that at present no definitive statement can be made as to whether or not the current data requirements in Annex II and III are sufficient to carry out risk assessments for nanopesticides[5]. Such assessments would likely require substantial efforts and resources, and a specific mandate would be necessary.

REFERENCES

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EFSA (2009a). Scientific Opinion of the Scientific Committee on "Existing approaches incorporating replacement, reduction and refinement of animal testing: applicability in food and feed risk assessment, 8 April 2009, *The EFSA Journal* (2009) 1052, 1-77.

EFSA (2009b) Scientific Opinion of the Scientific Committee on the potential risks arising from nanoscience and nanotechnologies on food and feed Safety, 10 February 2009, *The EFSA Journal* (2009) 958, 1-39.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2006. Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies. Adopted by the SCENIHR during the 10th plenary meeting of 10 March 2006 (after public consultation)[6].

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2007. Opinion on the scientific aspects of the existing and proposed definitions relating to products of nanoscience and nanotechnologies. Adopted by the SCENIHR at the 21st plenary meeting on 29 November 2007[7]. And accompanying information by Commission

[5] For a definition of nanomaterials, see EFSA 2009b
[6] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf
[7] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_012.pdf

services concerning the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) Opinion on the scientific aspects of the existing and proposed definitions relating to products of nanoscience and nanotechnologies[8].

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 2009. Opinion on risk assessment of products of nanotechnologies. Adopted by the SCENIHR during the 28th plenary meeting of 19 January 2009[9].

[8] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_oc_012.pdf
[9] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_023.pdf